WHAT IS CLAIMED IS:

1. A compound that binds to a cysteine residue in the RNA-dependent RNA polymerase (RdRp) protein of a virus forming a covalent bond.

2. A compound of Claim 1, wherein said RdRp protein is NS5B.

3. A compound of Claim 1, wherein said virus is hepatitis C virus (HCV).

4. A compound of Claim 1, wherein said cysteine residue corresponds to cysteine 366 in HCV NS5B.

5. A compound of Claim 1, wherein said RdRp is NS5B and said virus is HCV.

6. A compound of claim 5, wherein said covalent bond is irreversible under physiological conditions.

7. A compound of claim 5, wherein said covalent bond is reversible under physiological conditions.

8. A compound of claim 1, wherein said covalent bond results from a reaction selected from the group consisting of a Michael addition of said cysteine residue to an activated double or triple bond in said compound, an aromatic or aliphatic nucleophilic substitution reaction of said cysteine residue with an electrophilic center in said compound, a thioester forming reaction between said cysteine residue and a carboxylic acid or carboxylic acid derivative in said compound, a disulfide forming reaction between said cysteine residue and a sulfur-containing group in said compound, and a hemi-thioketal forming reaction between said cysteine residue and an activated or unactivated carbonyl group in said compound.

9. A compound useful for the covalent modification of a viral RNA-dependent RNA polymerase (RdRp) protein, said compound having the formula (**I**):

$$X^1\text{-}L^1\text{-}X^2\text{-}A\text{-}L^2\text{-}Ar^1$$

wherein

A is a electrophilic group that reacts with a cysteine residue of said RdRp protein;

Ar^1 is a member selected from the group consisting of substituted or unsubstituted aryl and substituted or unsubstituted heteroaryl;

X^1 is a member selected from the group consisting of -H, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, -CN, $-CO_2H$, $-SO_3H$, -C(O)NHOH, $-NH_2$, -OH, -NH(lower alkyl), -O(lower alkyl), -N(lower alkyl)$_2$, and –C(O)-NH(3-tetrazolyl);

L^1 is a divalent linking group selected from the group consisting of $-CH_2CH_2-$, -CH=CH-, -C≡C-, -O-, $-S(O)_n-$, $-N(R_a)-$, -C(O)-, -C(O)O-, $-SO_2N(R_a)-$, $-CON(R_a)-$, $-N(R_a)CON(R_b)-$, $-N(R_a)N(R_b)-$, $-N(R_a)SO_2N(R_b)-$, $-N(R_a)SO_2-$, $-N(R_a)-O-$, =N-O-, lower alkylene, -O-lower alkylene, $-S(O)_n-$lower alkylene, $N(R_a)$-lower alkylene, $-SO_2N(R_a)$-lower alkylene, lower alkylene-$SO_2N(R_a)-$, $-CON(R_a)$-lower alkylene, lower alkylene-$CON(R_a)-$, $-N(R_a)CON(R_b)$-lower alkylene, lower alkylene-$N(R_a)N(R_b)-$, $-N(R_a)SO_2N(R_b)$-lower alkylene, $-N(R_a)$-O-lower alkylene, lower alkylene-$N(R_a)-O-$, =N-O-lower alkylene, lower heteroalkylene, -O-lower heteroalkylene, $-S(O)_n-$lower heteroalkylene, $N(R_a)$-lower heteroalkylene, $-SO_2N(R_a)$-lower heteroalkylene, lower heteroalkylene-$SO_2N(R_a)-$, $-CON(R_a)$-lower heteroalkylene, lower heteroalkylene-$CON(R_a)-$, $-N(R_a)CON(R_b)$-lower heteroalkylene, lower heteroalkylene-$N(R_a)N(R_b)-$, $-N(R_a)SO_2N(R_b)$-lower heteroalkylene, $-N(R_a)$-O-lower heteroalkylene, lower heteroalkylene-$N(R_a)-O-$, =N-O-lower alkylene, aryl and heteroaryl;

X^2 is a member selected from the group consisting of substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, and substituted or unsubstituted heterocycloalkyl;

L^2 is a divalent linking group selected from the group consisting of $-CH_2CH_2-$, $-(C(R_c)=C(R_d))_m-$, -O-, $-S(O)_n-$, $-N(R_e)-$, -C(O)-, -C(O)O-, $-SO_2N(R_e)-$, $-CON(R_e)-$, $-N(R_e)CON(R_f)-$, $-N(R_e)N(R_f)-$, $-N(R_e)SO_2N(R_f)-$, $-N(R_e)-O-$, =N-O-, lower alkylene, perfluoro lower alkylene, polyfluoro lower alkylene, -O-lower alkylene, $-S(O)_n-$lower alkylene, $N(R_e)$-lower alkylene, $-SO_2N(R_e)$-lower alkylene, lower alkylene-$SO_2N(R_e)-$, $-CON(R_e)$-lower alkylene, lower alkylene-$CON(R_e)-$, $-N(R_e)CON(R_f)$-lower alkylene, lower alkylene-$N(R_e)N(R_f)-$, $-N(R_e)SO_2N(R_f)$-lower alkylene, $-N(R_e)$-O-lower alkylene, lower alkylene-$N(R_e)-O-$, =N-O-lower alkylene,

lower heteroalkylene, -O-lower heteroalkylene, -$S(O)_n$-lower heteroalkylene, $N(R_e)$-lower heteroalkylene, -$SO_2N(R_e)$-lower heteroalkylene, lower heteroalkylene-$SO_2N(R_e)$-, -$CON(R_e)$-lower heteroalkylene, lower heteroalkylene-$CON(R_e)$-, -$N(R_e)CON(R_f)$-lower heteroalkylene, lower heteroalkylene-$N(R_e)N(R_f)$-, -$N(R_e)SO_2N(R_f)$-lower heteroalkylene, -$N(R_e)$-O-lower heteroalkylene, lower heteroalkylene-$N(R_e)$-O-, =N-O-lower alkylene, aryl and heteroaryl, wherein R_a, R_b, R_c, R_d, R_e and R_f are each members independently selected from the group consisting of H, lower alkyl, lower heteroalkyl, -C(O)-lower alkyl, -C(O)-lower heteroalkyl, $-S(O)_2$-lower alkyl, and $-S(O)_2$-lower heteroalkyl;

the subscript n is an integer of from 0 to 2;

the subscript m is an integer of from 0 to 3;

the bond between X^2 and A can be a single, double or triple bond, depending on the nature of X^2 and A; and

wherein when L^1 and L^2 may be linked together *via* a single bond, -O-, -S- or amide group to form a new 5 to 7 membered ring;

with the proviso that when A is an sp^2-hybridized carbon atom and X^2 is substituted or unsubstituted rhodanine, L^1 is not $-CH_2-CH_2-$, -CH=CH-, -C≡C- or aryl.

10. A compound in accordance with claim 9, wherein

X^2 is selected from the group consisting of a 5 to 7 membered cycloalkyl ring, a 5 to 7 membered heterocycloalkyl ring containing from 1 to 3 heteroatoms, an aryl group and a heteroaryl group;

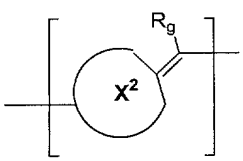
A is selected from the group consisting of an sp^2-hybridized carbon atom and an sp^3-hybridized carbon atom;

L^2 is a single bond; and

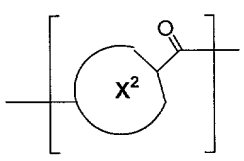
X^2 and A are joined *via* a single or double bond.

11. A compound in accordance with claim 10, wherein

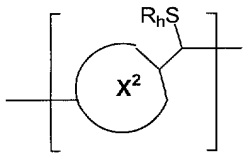
X^2-A- is selected from the group consisting of:



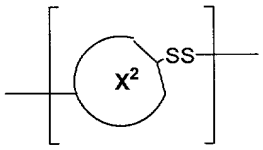
$[X^2\text{-}A]_a$,



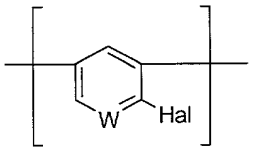
$[X^2\text{-}A]_b$,



$[X^2\text{-}A]_c$,



$[X^2\text{-}A]_d$ and



$[X^2\text{-}A]_e$

wherein R_g is selected from the group consisting of H, lower alkyl, lower alkoxy and F; R_h is selected from the group consisting of H, -$S(O)_n$-lower alkyl, -$S(O)_n$-lower heteroalkyl, -$S(O)_n$-aryl and -$S(O)_n$-heteroaryl;

W is CH or N; Hal is a halogen atom; and

X^2 is a substituted or unsubstituted member selected from the group consisting of a 5-6 membered cycloalkyl, 5-6 membered heterocycloalkyl containing from 1 to 3 heteroatoms, heteroaryl containing from 1 to 3 heteroatoms and aryl.

12. A compound having the formula (**II**):

$$X^1\text{-}L^1\text{-}B\text{-}L^2\text{-}Ar^1$$

wherein

Ar^1 is a member selected from the group consisting of substituted or unsubstituted aryl and substituted or unsubstituted heteroaryl;

X^1 is a member selected from the group consisting of -H, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, -CN, -CO_2H, -SO_3H, -C(O)NHOH, -NH_2, -OH, -NH(lower alkyl), -O(lower alkyl), -N(lower alkyl)$_2$, and –C(O)-NH(3-tetrazolyl);

L^1 is a divalent linking group selected from the group consisting of -CH_2CH_2-, -CH=CH-, -C≡C-, -O-, -$S(O)_n$-, -$N(R_a)$-, -C(O)-, -C(O)O-, -$SO_2N(R_a)$-, -$CON(R_a)$-, -$N(R_a)CON(R_b)$-, -$N(R_a)N(R_b)$-, -$N(R_a)SO_2N(R_b)$-, -$N(R_a)SO_2$-, -$N(R_a)$-O-, =N-O-, lower alkylene, -O-lower alkylene, -$S(O)_n$-lower alkylene, $N(R_a)$-lower alkylene, -$SO_2N(R_a)$-lower alkylene, lower alkylene-$SO_2N(R_a)$-, -$CON(R_a)$-lower alkylene, lower alkylene-$CON(R_a)$-, -$N(R_a)CON(R_b)$-lower alkylene, lower alkylene-$N(R_a)N(R_b)$-, -$N(R_a)SO_2N(R_b)$-lower alkylene, -$N(R_a)$-O-lower alkylene, lower alkylene-$N(R_a)$-O-,

=N-O-lower alkylene, lower heteroalkylene, -O-lower heteroalkylene, -$S(O)_n$-lower heteroalkylene, $N(R_a)$-lower heteroalkylene, -$SO_2N(R_a)$-lower heteroalkylene, lower heteroalkylene-$SO_2N(R_a)$-, -$CON(R_a)$-lower heteroalkylene, lower heteroalkylene-$CON(R_a)$-, -$N(R_a)CON(R_b)$-lower heteroalkylene, lower heteroalkylene-$N(R_a)N(R_b)$-, -$N(R_a)SO_2N(R_b)$-lower heteroalkylene, -$N(R_a)$-O-lower heteroalkylene, lower heteroalkylene-$N(R_a)$-O-, =N-O-lower alkylene, aryl and heteroaryl;

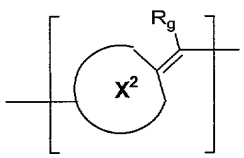
L^2 is a divalent linking group selected from the group consisting of -CH_2CH_2-, -$(C(R_c)=C(R_d))_m$-, -O-, -$S(O)_n$-, -$N(R_e)$-, -C(O)-, -C(O)O-, -$SO_2N(R_e)$-, -$CON(R_e)$-, -$N(R_e)CON(R_f)$-, -$N(R_e)N(R_f)$-, -$N(R_e)SO_2N(R_f)$-, -$N(R_e)$-O-, =N-O-, lower alkylene, perfluoro lower alkylene, polyfluoro lower alkylene, -O-lower alkylene, -$S(O)_n$-lower alkylene, $N(R_e)$-lower alkylene, -$SO_2N(R_e)$-lower alkylene, lower alkylene-$SO_2N(R_e)$-, -$CON(R_e)$-lower alkylene, lower alkylene-$CON(R_e)$-, -$N(R_e)CON(R_f)$-lower alkylene, lower alkylene-$N(R_e)N(R_f)$-, -$N(R_e)SO_2N(R_f)$-lower alkylene, -$N(R_e)$-O-lower alkylene, lower alkylene-$N(R_e)$-O-, =N-O-lower alkylene, lower heteroalkylene, -O-lower heteroalkylene, -$S(O)_n$-lower heteroalkylene, $N(R_e)$-lower heteroalkylene, -$SO_2N(R_e)$-lower heteroalkylene, lower heteroalkylene-$SO_2N(R_e)$-, -$CON(R_e)$-lower heteroalkylene, lower heteroalkylene-$CON(R_e)$-, -$N(R_e)CON(R_f)$-lower heteroalkylene, lower heteroalkylene-$N(R_e)N(R_f)$-, -$N(R_e)SO_2N(R_f)$-lower heteroalkylene, -$N(R_e)$-O-lower heteroalkylene, lower heteroalkylene-$N(R_e)$-O-, =N-O-lower alkylene, aryl and heteroaryl, wherein R_a, R_b, R_c, R_d, R_e and R_f are each members independently selected from the group consisting of H, lower alkyl, lower heteroalkyl, -C(O)-lower alkyl, -C(O)-lower heteroalkyl, –$S(O)_2$-lower alkyl, and –$S(O)_2$-lower heteroalkyl;

the subscript n is an integer of from 0 to 2;

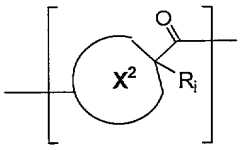
the subscript m is an integer of from 0 to 3;

B is selected from the group consisting of:

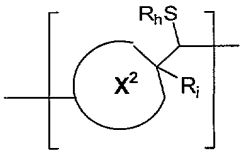
09825270 - 050502



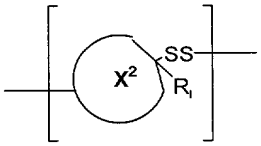
B_a



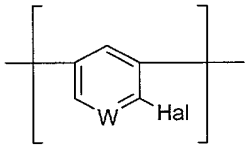
B_b



B_c

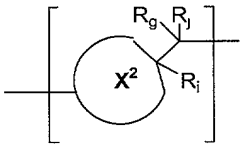


B_c



B_e

and



B_f ;

wherein X^2 is a substituted or unsubstituted member selected from the group consisting of a 5-6 membered cycloalkyl, 5-6 membered heterocycloalkyl containing from 1 to 3 heteroatoms, heteroaryl containing from 1 to 3 heteroatoms and aryl;

W is CH or N;

R_g is selected from the group consisting of H, lower alkyl, lower alkoxy and F;

R_h is selected from the group consisting of H, $-S(O)_n$-lower alkyl, $-S(O)_n$-lower heteroalkyl, $-S(O)_n$-aryl and $-S(O)_n$-heteroaryl;

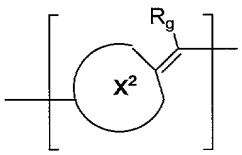
R_i is selected from the group consisting of H, lower alkyl, lower heteroalkyl, or a bond that links the atom bearing R_i with another atom in the X^2 ring;

R_j is selected from the group consisting of H, lower alkyl, F and lower alkoxy; and

Hal is a halogen atom;

wherein when L^1 and L^2 may be linked together *via* a single bond, -O-, -S- or amide group to form a new 5 to 7 membered ring;

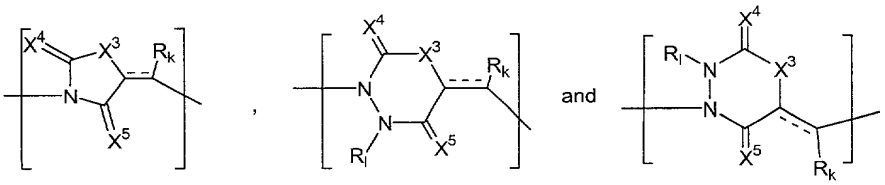
with the proviso that when B is



B_a

65 and X^2 is rhodanine, L^1 is not $-CH_2-CH_2-$, -CH=CH-, -C≡C- or aryl.

1 **13.** A compound in accordance with claim **12**, wherein B is selected
2 from the group consisting of:



3 B_g B_h B_i

4 wherein

5 R_k is selected from the group consisting of H, lower alkyl, lower
6 heteroalkyl and F;

7 R_l is H or lower alkyl;

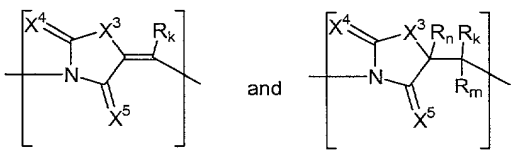
8 X^3 is selected from the group consisting of O, S, CH_2, CH(lower alkyl),
9 C(lower alkyl)$_2$, NH and N(lower alkyl);

10 X^4 is selected from the group consisting of O, S, NH and N(lower alkyl),
11 or X^4 and the carbon atom to which it is attached represents an sp^3-hybridized carbon
12 having two substituents independently selected from the group consisting of H, lower
13 alkyl and lower heteroalkyl;

14 X^5 is selected from the group consisting of O, S, NH and N(lower alkyl),
15 or X^5 and the carbon atom to which it is attached represents an sp^3-hybridized carbon
16 having two substituents independently selected from the group consisting of H, lower
17 alkyl, lower alkoxy, aryloxy, lower thioalkoxy and arylthioxy; and

18 ___ represents either a single or double bond, with the proviso that when a
19 single bond is intended, the ring atom bearing said single bond bears an additional
20 substituent selected from the group consisting of H, lower alkyl, lower alkoxy and F.

1 **14.** A compound of claim **13**, wherein B is selected from the group
2 consisting of:



3 B_j B_k

4 wherein

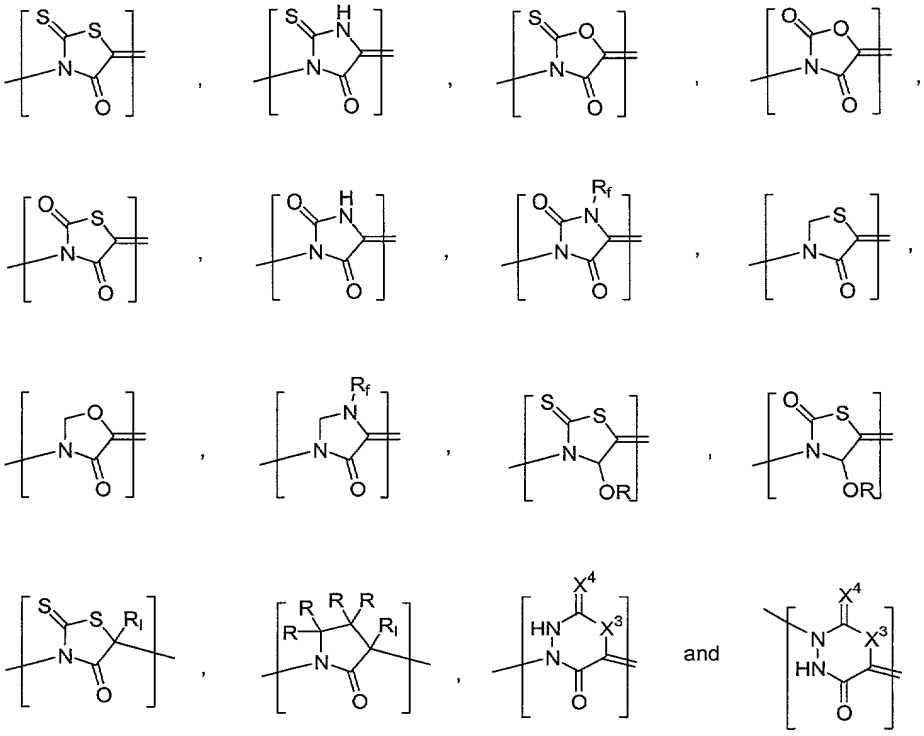
R_k, R_m and R_n are each independently selected from the group consisting of H, F, lower alkyl and lower alkoxy;

X^3 is selected from the group consisting of O, S, C(lower alkyl)$_2$, NH and N(lower alkyl);

X^4 is selected from the group consisting of O and S, or X^4 and the carbon atom to which it is attached represents an sp^3-hybridized carbon having two substituents independently selected from the group consisting of H, lower alkyl and lower heteroalkyl;

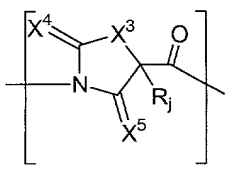
X^5 is selected from the group consisting of O and S, or X^5 and the carbon atom to which it is attached represents an sp^3-hybridized carbon having two substituents independently selected from the group consisting of H, lower alkoxy and lower thioalkoxy.

15. A compound of claim **14**, wherein B is selected from the group consisting of:

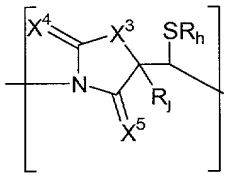


wherein any unlabeled R groups are independently selected from the group consisting of H, lower alkyl, lower alkoxy and F.

16. A compound of claim **12** wherein B is selected from the group consisting of:

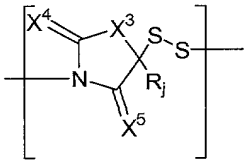


B_l



B_m

and



B_n

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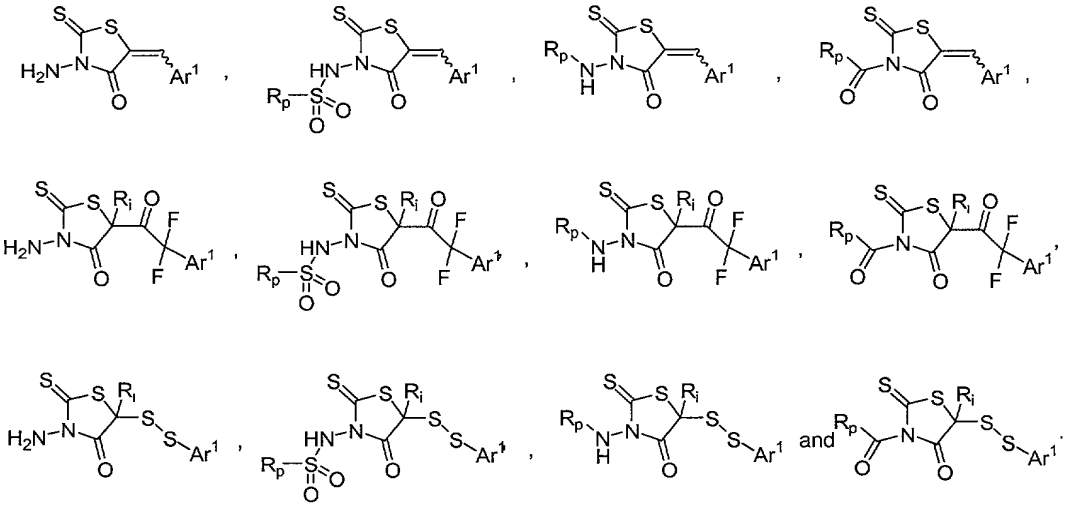
17. A compound of claim **12**, wherein L^1 is selected from the group consisting of $-N(R_a)-$, $-N(R_a)$-alkylene, alkylene-$SO_2-N(R_a)-$, $-SO_2-N(R_a)-$ and $-N(R_a)SO_2-$; and X^1 is selected from the group consisting of H, aryl and alkyl.

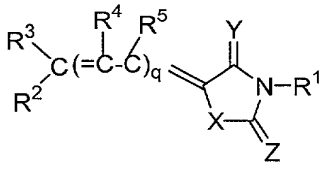
18. A compound of claim **12**, wherein Ar^1 is selected from the group consisting of substituted or unsubstituted biphenyl group, substituted or unsubstituted bicyclic ring, substituted or unsubstituted phenyl group and substituted or unsubstituted pyridyl.

19. A compound of claim **17**, said compound having the formula:



wherein R_p is selected from the group consisting of substituted or unsubstituted alkyl, substituted or unsubstituted aryl and substituted or unsubstituted heteroaryl.

20. A compound of Claim **12**, said compound having the formula (**III**):



wherein

the subscript q is an integer of from 0 to 4;

R^1 is hydrogen or a substituent having the formula $-L^1$-COOH;

X is a moiety selected from –S-, -O-, and -N(R_o)- , wherein R_o is H or lower alkyl;

R^2 is a substituted or unsubstituted aryl(C_1-C_8)alkyl, a substituted or unsubstituted aryl(C_1-C_8)alkenyl, a substituted or unsubstituted aryl(C_1-C_8)alkynyl, a substituted or unsubstituted alicyclic group having from 5-8 carbon atoms, or a group having the formula $(R_{2a})_r$-$(L)_s$-R_{2b}-, wherein R_{2a} and R_{2b} can be the same or different and represent a substituted or unsubstituted heterocyclic group or a substituted or unsubstituted phenyl group, R_{2a} can also represent a substituted or unsubstituted polycyclic group, and L represents a divalent linking group selected from methylene, ethylene, propylene, -CH=CH-, -C≡C-, -C(O)-, -O-, -S-, -S(O)-, -$S(O)_2$-, or –N(R_{2c})-, wherein R_{2c} is selected from H or lower alkyl, and the subscripts r and s are each independently 0 or 1;

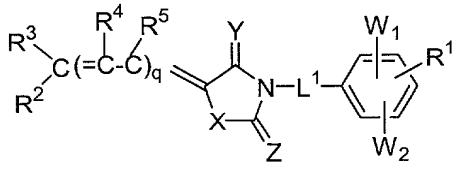
R^3 is selected from the group consisting of H, substituted or unsubstituted (C_1-C_8)alkyl, substituted and unsubstituted aryl or substituted and unsubstituted heteroaryl;

Y represents O or S; and

Z represents O, S or N(R_{2d}), wherein R_{2d} is H or lower alkyl, or R_{2d} and R^1 may be joined to form an imidazole or benzimidazole group;

with the proviso that when R^1 is hydrogen, R^3 is not substituted furan.

21. A compound of Claim **12**, said compound having the formula (**V**):



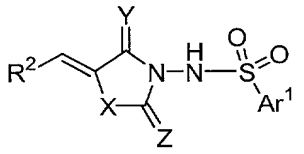
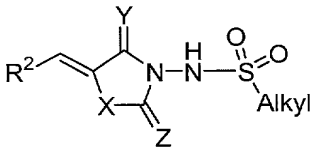
wherein

R^1 is H, -OH, -$COOR_u$, -$CONR_vR_w$, -$SO_2NR_xR_y$ wherein R_u, R_v, R_w, R_x and R_y are H or lower alkyl, or R^1 is a mono-heterocyclic group selected from furan, thiophene, pyridine, pyrimidine, pyridazine, 1,3-oxathiolane, tetrazole, oxadiazole, oxazole, triazole, imidazoline, imidazole, thiazole, thiadiazole, pyrrole, piperidine, morpholine, triazine and pyrazole; and

W_1 and W_2 are independently selected from H, (C_1-C_8)alkyl, (C_1-C_8)alkenyl, (C_1-C_8)alkynyl, halogen, nitro, hydroxy, perfluoroalkyl, difluoromethyl, (C_1-

C_8)alkoxy, phenoxy, phenyl(C_1-C_8)alkoxy, (C_1-C_8)acyl, (C_1-C_8)acyloxy, cyano, carbalkoxy, thio, (C_1-C_8)alkylthio, (C_1-C_8)alkylsulfinyl, (C_1-C_8)alkylsulfonyl, amino, (C_1-C_8)alkylamino, di(C_1-C_8)alkylamino, sulfonamido, carboxamido and (C_1-C_8)alkanoylamino.

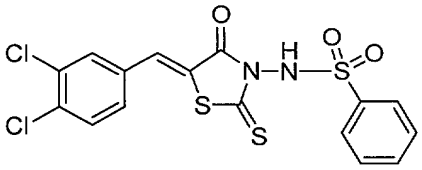
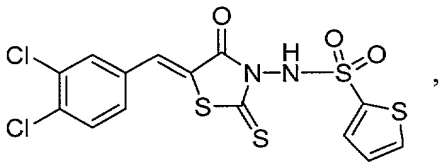
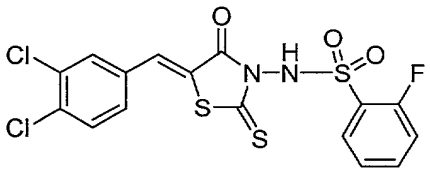
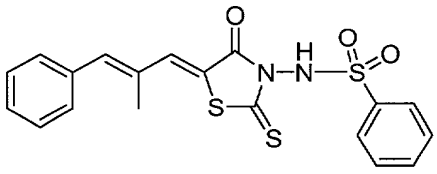
22. A compound of Claim **12**, said compound having a formula selected from the group consisting of


and


wherein

R^2 is a substituted or unsubstituted mono- or bi-heterocyclic group, a substituted or unsubstituted polycyclic ring, a substituted or unsubstituted alicyclic group having 5-8 carbon atoms, a substituted or unsubstituted phenyl group, a substituted or unsubstituted biphenyl group, a substituted or unsubstituted phenylether group, a substituted or unsubstituted cinnamenyl group, or a substituted or unsubstituted stilbenyl group.

23. The compound of Claim **22**, wherein said compound is selected from the group consisting of


,

,

and

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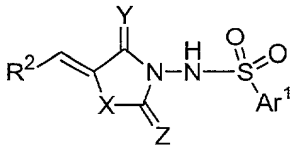
24. A compound having the formula (**VIIa**):



wherein

Ar^1 is selected from the group consisting of substituted or unsubstituted aryl and substituted or unsubstituted heteroaryl;

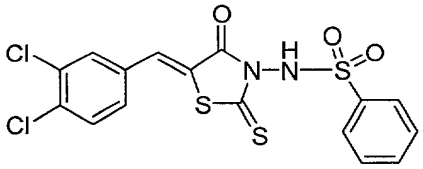
X is selected from –S-, -O- and -$N(R_o)$- , wherein R_o is H or lower alkyl;

Y is O or S; and

Z is O, S or $N(R_{2d})$, wherein R_{2d} is H or lower alkyl, or R_{2d} and R^1 may be joined to form an imidazole or benzimidazole group; and

R^2 is a substituted or unsubstituted mono- or bi-heterocyclic group, a substituted or unsubstituted polycyclic ring, a substituted or unsubstituted alicyclic group having 5-8 carbon atoms, a substituted or unsubstituted phenyl group, a substituted or unsubstituted biphenyl group, a substituted or unsubstituted phenylether group, a substituted or unsubstituted cinnamenyl group, or a substituted or unsubstituted stilbenyl group.

25. The compound of Claim **24**, wherein said compound is selected from the group consisting of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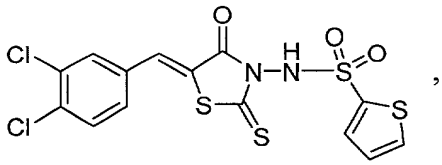
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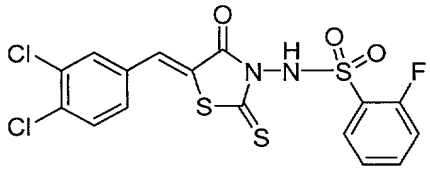
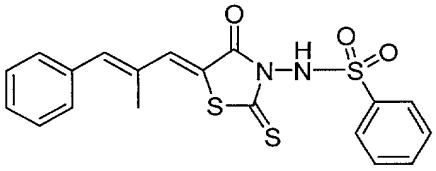

and

.

26. A compound useful for the covalent modification of a viral RNA-dependent RNA polymerase (RdRp) protein, said compound having the formula:

$$X^1\text{-}L^1\text{-}X^2\text{-}A\text{-}L^2\text{-}Ar^1$$

wherein

A is a electrophilic group that reacts with a cysteine residue of said viral RNA-dependent RNA polymerase protein;

Ar^1 is a member selected from the group consisting of substituted or unsubstituted aryl and substituted or unsubstituted heteroaryl;

X^1 is a member selected from the group consisting of -H, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, -CN, $-CO_2H$, $-SO_3H$, -C(O)NHOH, $-NH_2$, -OH, -NH(lower alkyl), -O(lower alkyl), -N(lower alkyl)$_2$, and –C(O)-NH(3-tetrazolyl);

L^1 is a divalent linking group selected from the group consisting of -O-, $-S(O)_n-$, $-N(R_a)-$, -C(O)-, -C(O)O-, $-SO_2N(R_a)-$, $-CON(R_a)-$, $-N(R_a)CON(R_b)-$, $-N(R_a)N(R_b)-$, $-N(R_a)SO_2N(R_b)-$, $-N(R_a)SO_2-$, $-N(R_a)-O-$, =N-O-, lower alkylene, -O-lower alkylene, $-S(O)_n-$lower alkylene, $N(R_a)$-lower alkylene, $-SO_2N(R_a)$-lower alkylene, lower alkylene-$SO_2N(R_a)-$, $-CON(R_a)$-lower alkylene, lower alkylene-$CON(R_a)-$, $-N(R_a)CON(R_b)$-lower alkylene, lower alkylene-$N(R_a)N(R_b)-$, $-N(R_a)SO_2N(R_b)$-lower alkylene, $-N(R_a)$-O-lower alkylene, lower alkylene-$N(R_a)-O-$, =N-O-lower alkylene, lower heteroalkylene, -O-lower heteroalkylene, $-S(O)_n-$lower heteroalkylene, $N(R_a)$-lower heteroalkylene, $-SO_2N(R_a)$-lower heteroalkylene, lower heteroalkylene-$SO_2N(R_a)-$, $-CON(R_a)$-lower heteroalkylene, lower heteroalkylene-$CON(R_a)-$, $-N(R_a)CON(R_b)$-lower heteroalkylene, lower heteroalkylene-$N(R_a)N(R_b)-$, $-N(R_a)SO_2N(R_b)$-lower heteroalkylene, $-N(R_a)$-O-lower heteroalkylene, lower heteroalkylene-$N(R_a)-O-$, =N-O-lower alkylene and heteroaryl;

X^2 is a member selected from the group consisting of substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, and substituted or unsubstituted heterocycloalkyl;

L^2 is a divalent linking group selected from the group consisting of $-CH_2CH_2-$, $-(C(R_c)=C(R_d))_m-$, -O-, $-S(O)_n-$, $-N(R_e)-$, -C(O)-, -C(O)O-, $-SO_2N(R_e)-$, $-CON(R_e)-$, $-N(R_e)CON(R_f)-$, $-N(R_e)N(R_f)-$, $-N(R_e)SO_2N(R_f)-$, $-N(R_e)-O-$, =N-O-, lower alkylene, perfluoro lower alkylene, polyfluoro lower alkylene, -O-lower alkylene, $-S(O)_n-$lower alkylene, $N(R_e)$-lower alkylene, $-SO_2N(R_e)$-lower alkylene, lower alkylene-$SO_2N(R_e)-$, $-CON(R_e)$-lower alkylene, lower alkylene-$CON(R_e)-$, $-N(R_e)CON(R_f)$-lower alkylene, lower alkylene-$N(R_e)N(R_f)-$, $-N(R_e)SO_2N(R_f)$-lower alkylene, $-N(R_e)$-O-lower alkylene, lower alkylene-$N(R_e)-O-$, =N-O-lower alkylene, lower heteroalkylene, -O-lower heteroalkylene, $-S(O)_n-$lower heteroalkylene, $N(R_e)$-lower heteroalkylene, $-SO_2N(R_e)$-lower heteroalkylene, lower heteroalkylene-$SO_2N(R_e)-$, $-CON(R_e)$-lower heteroalkylene, lower heteroalkylene-$CON(R_e)-$, $-N(R_e)CON(R_f)$-lower heteroalkylene, lower heteroalkylene-$N(R_e)N(R_f)-$, $-N(R_e)SO_2N(R_f)$-lower heteroalkylene, $-N(R_e)$-O-lower heteroalkylene, lower heteroalkylene-$N(R_e)-O-$, =N-O-lower alkylene, aryl and heteroaryl;

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wherein R_a, R_b, R_c, R_d, R_e and R_f are each members independently selected from the group consisting of H, lower alkyl, lower heteroalkyl, -C(O)-lower alkyl, -C(O)-lower heteroalkyl, $-S(O)_2$-lower alkyl, and $-S(O)_2$-lower heteroalkyl;

the subscript n is an integer of from 0 to 2;

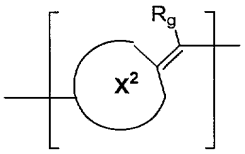
the subscript m is an integer of from 0 to 3;

the bond between X^2 and A can be a single, double or triple bond, depending on the nature of X^2 and A; and

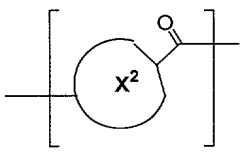
wherein when L^1 and L^2 may be linked together *via* a single bond, -O-, -S- or amide group to form a new 5 to 7 membered ring.

27. A compound in accordance with claim **26**, wherein X^2 is selected from the group consisting of a 5 to 7 membered cycloalkyl ring, a 5 to 7 membered heterocycloalkyl ring containing from 1 to 3 heteroatoms, an aryl group and a heteroaryl group; A is selected from the group consisting of an sp^2-hybridized carbon atom and an sp^3-hybridized carbon atom; L^2 is a single bond; and X^2 and A are joined *via* a single or double bond.

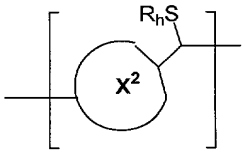
28. A compound in accordance with claim **27**, wherein $-X^2$-A- is selected from the group consisting of:



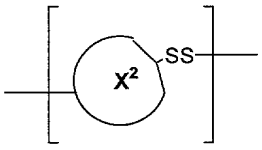
$[X^2\text{-}A]_a$,



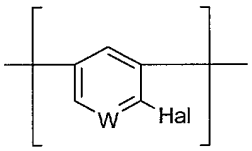
$[X^2\text{-}A]_b$,



$[X^2\text{-}A]_c$,



$[X^2\text{-}A]_d$ and



$[X^2\text{-}A]_e$

wherein R_g is selected from the group consisting of H, lower alkyl, lower alkoxy and F;

R_h is selected from the group consisting of H, $-S(O)_n$-lower alkyl, $-S(O)_n$-lower heteroalkyl, $-S(O)_n$-aryl and $-S(O)_n$-heteroaryl; W is CH or N; Hal is a halogen atom; and X^2 is a substituted or unsubstituted member selected from the group consisting

of a 5-6 membered cycloalkyl, 5-6 membered heterocycloalkyl containing from 1 to 3 heteroatoms, heteroaryl containing from 1 to 3 heteroatoms and aryl.

29. A compound having the formula (**II**):

$$X^1\text{-}L^1\text{-}B\text{-}L^2\text{-}Ar^1$$

wherein

Ar^1 is a member selected from the group consisting of substituted or unsubstituted aryl and substituted or unsubstituted heteroaryl;

X^1 is a member selected from the group consisting of -H, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, -CN, $-CO_2H$, $-SO_3H$, -C(O)NHOH, $-NH_2$, -OH, -NH(lower alkyl), -O(lower alkyl), -N(lower alkyl)$_2$, and –C(O)-NH(3-tetrazolyl);

L^1 is a divalent linking group selected from the group consisting of -O-, $-S(O)_n$-, $-N(R_a)$-, -C(O)-, -C(O)O-, $-SO_2N(R_a)$-, $-CON(R_a)$-, $-N(R_a)CON(R_b)$-, $-N(R_a)N(R_b)$-, $-N(R_a)SO_2N(R_b)$-, $-N(R_a)SO_2$-, $-N(R_a)$-O-, =N-O-, lower alkylene, -O-lower alkylene, $-S(O)_n$-lower alkylene, $N(R_a)$-lower alkylene, $-SO_2N(R_a)$-lower alkylene, lower alkylene-$SO_2N(R_a)$-, $-CON(R_a)$-lower alkylene, lower alkylene-$CON(R_a)$-, $-N(R_a)CON(R_b)$-lower alkylene, lower alkylene-$N(R_a)N(R_b)$-, $-N(R_a)SO_2N(R_b)$-lower alkylene, $-N(R_a)$-O-lower alkylene, lower alkylene-$N(R_a)$-O-, =N-O-lower alkylene, lower heteroalkylene, -O-lower heteroalkylene, $-S(O)_n$-lower heteroalkylene, $N(R_a)$-lower heteroalkylene, $-SO_2N(R_a)$-lower heteroalkylene, lower heteroalkylene-$SO_2N(R_a)$-, $-CON(R_a)$-lower heteroalkylene, lower heteroalkylene-$CON(R_a)$-, $-N(R_a)CON(R_b)$-lower heteroalkylene, lower heteroalkylene-$N(R_a)N(R_b)$-, $-N(R_a)SO_2N(R_b)$-lower heteroalkylene, $-N(R_a)$-O-lower heteroalkylene, lower heteroalkylene-$N(R_a)$-O-, =N-O-lower alkylene and heteroaryl;

L^2 is a divalent linking group selected from the group consisting of $-CH_2CH_2$-, $-(C(R_c)=C(R_d))_m$-, -O-, $-S(O)_n$-, $-N(R_e)$-, -C(O)-, -C(O)O-, $-SO_2N(R_e)$-, $-CON(R_e)$-, $-N(R_e)CON(R_f)$-, $-N(R_e)N(R_f)$-, $-N(R_e)SO_2N(R_f)$-, $-N(R_e)$-O-, =N-O-, lower alkylene, perfluoro lower alkylene, polyfluoro lower alkylene, -O-lower alkylene, $-S(O)_n$-lower alkylene, $N(R_e)$-lower alkylene, $-SO_2N(R_e)$-lower alkylene, lower alkylene-$SO_2N(R_e)$-, $-CON(R_e)$-lower alkylene, lower alkylene-$CON(R_e)$-, $-N(R_e)CON(R_f)$-lower alkylene, lower alkylene-$N(R_e)N(R_f)$-, $-N(R_e)SO_2N(R_f)$-lower alkylene, $-N(R_e)$-O-lower alkylene, lower alkylene-$N(R_e)$-O-, =N-O-lower alkylene,

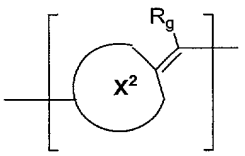
lower heteroalkylene, -O-lower heteroalkylene, -S(O)$_n$-lower heteroalkylene, N(R_e)-lower heteroalkylene, -SO_2N(R_e)-lower heteroalkylene, lower heteroalkylene-SO_2N(R_e)-, -CON(R_e)-lower heteroalkylene, lower heteroalkylene-CON(R_e)-, -N(R_e)CON(R_f)-lower heteroalkylene, lower heteroalkylene-N(R_e)N(R_f)-, -N(R_e)SO_2N(R_f)-lower heteroalkylene, -N(R_e)-O-lower heteroalkylene, lower heteroalkylene-N(R_e)-O-, =N-O-lower alkylene, aryl and heteroaryl;

wherein R_a, R_b, R_c, R_d, R_e and R_f are each members independently selected from the group consisting of H, lower alkyl, lower heteroalkyl, -C(O)-lower alkyl, -C(O)-lower heteroalkyl, –S(O)$_2$-lower alkyl, and –S(O)$_2$-lower heteroalkyl;

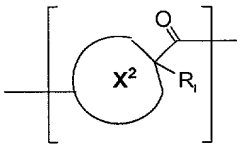
the subscript n is an integer of from 0 to 2;

the subscript m is an integer of from 0 to 3;

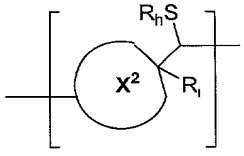
B is selected from the group consisting of:



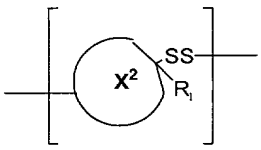
B_a ,



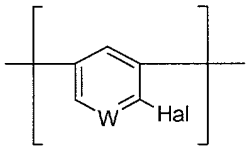
B_b ,



B_c ,

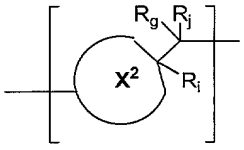


B_c



B_e

and



B_f ;

wherein

X^2 is a substituted or unsubstituted member selected from the group consisting of a 5-6 membered cycloalkyl, 5-6 membered heterocycloalkyl containing from 1 to 3 heteroatoms, heteroaryl containing from 1 to 3 heteroatoms and aryl;

W is CH or N;

R_g is selected from the group consisting of H, lower alkyl, lower alkoxy and F;

R_h is selected from the group consisting of H, -S(O)$_n$-lower alkyl, -S(O)$_n$-lower heteroalkyl, -S(O)$_n$-aryl and -S(O)$_n$-heteroaryl;

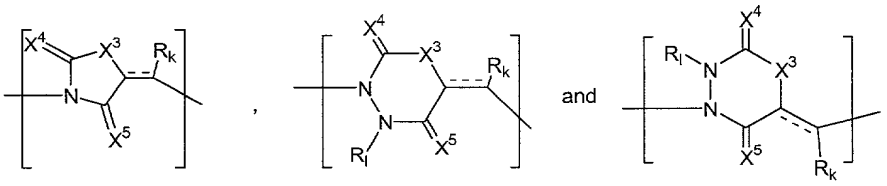
R_i is selected from the group consisting of H, lower alkyl, lower heteroalkyl, or a bond that links the atom bearing R_i with another atom in the X^2 ring;

R_j is selected from the group consisting of H, lower alkyl, F and lower alkoxy; and

Hal is a halogen atom;

wherein when L^1 and L^2 may be linked together *via* a single bond, -O-, -S- or amide group to form a new 5 to 7 membered ring.

30. A compound in accordance with claim **29**, wherein B is selected from the group consisting of:



B_g B_h B_i

wherein

R_k is selected from the group consisting of H, lower alkyl, lower heteroalkyl and F;

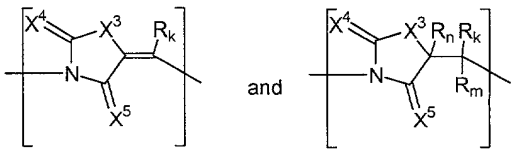
R_l is H or lower alkyl;

X^3 is selected from the group consisting of O, S, CH_2, CH(lower alkyl), $C(\text{lower alkyl})_2$, NH and N(lower alkyl);

X^4 is selected from the group consisting of O, S, NH and N(lower alkyl), or X^4 and the carbon atom to which it is attached represents an sp^3-hybridized carbon having two substituents independently selected from the group consisting of H, lower alkyl and lower heteroalkyl; and

X^5 is selected from the group consisting of O, S, NH and N(lower alkyl), or X^5 and the carbon atom to which it is attached represents an sp^3-hybridized carbon having two substituents independently selected from the group consisting of H, lower alkyl, lower alkoxy, aryloxy, lower thioalkoxy and arylthioxy; and - - - represents either a single or double bond, with the proviso that when a single bond is intended, the ring atom bearing said single bond bears an additional substituent selected from the group consisting of H, lower alkyl, lower alkoxy and F.

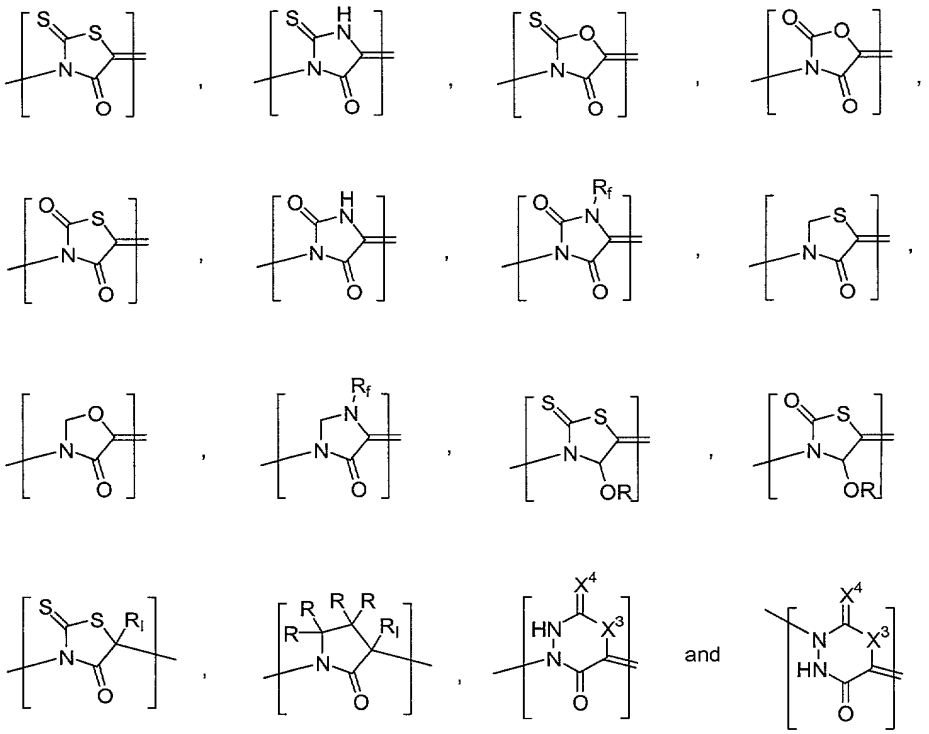
31. A compound of claim **30**, wherein B is selected from the group consisting of:



B_j B_k

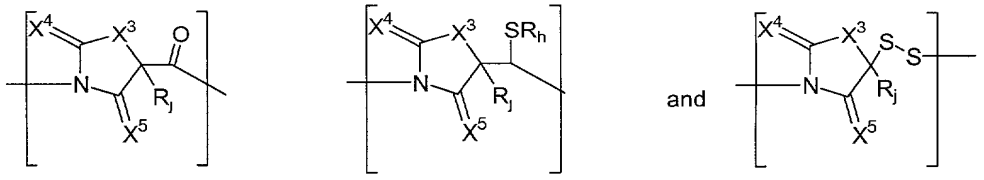
wherein R_k, R_m and R_n are each independently selected from the group consisting of H, F, lower alkyl and lower alkoxy; X^3 is selected from the group consisting of O, S, C(lower alkyl)$_2$, NH and N(lower alkyl); X^4 is selected from the group consisting of O, S, or X^4 and the carbon atom to which it is attached represents an sp^3-hybridized carbon having two substituents independently selected from the group consisting of H, lower alkyl and lower heteroalkyl; X^5 is selected from the group consisting of O, S, or X^5 and the carbon atom to which it is attached represents an sp^3-hybridized carbon having two substituents independently selected from the group consisting of H, lower alkoxy and lower thioalkoxy.

32. A compound of claim **31**, wherein B is selected from the group consisting of:



wherein any unlabeled R groups are independently selected from the group consisting of H, lower alkyl, lower alkoxy and F.

33. A compound of claim **29**, wherein B is selected from the group consisting of:

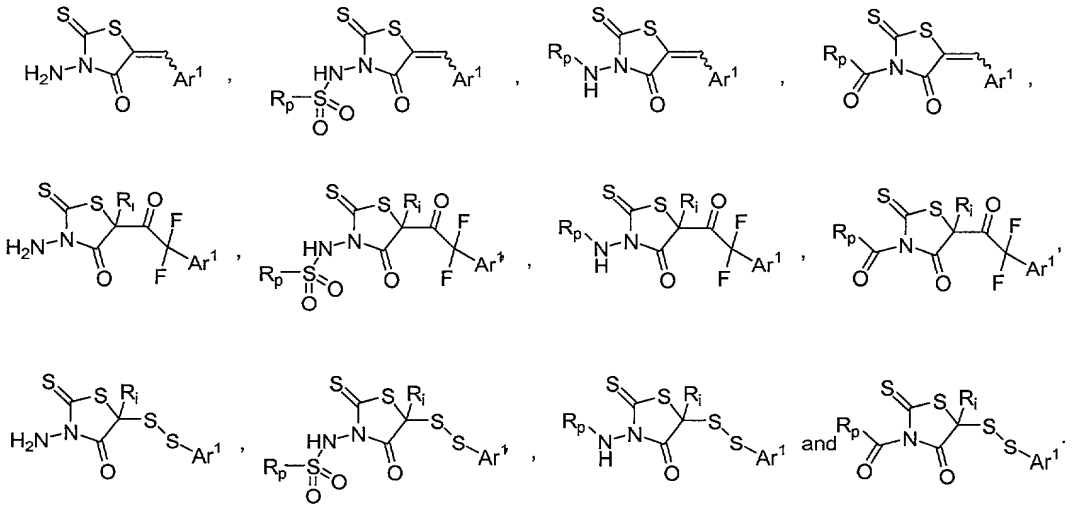


B_l B_m and B_n

34. A compound of claim **29** wherein L^1 is selected from the group consisting of $-N(R_a)-$, $-N(R_a)$-alkylene, alkylene-$SO_2-N(R_a)-$, $-SO_2-N(R_a)-$ and $-N(R_a)SO_2-$; and X^1 is selected from the group consisting of H, aryl and alkyl.

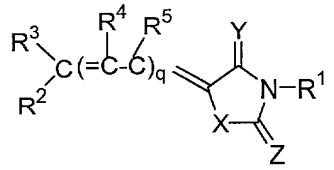
35. A compound of claim **29**, wherein Ar^1 is selected from the group consisting of substituted or unsubstituted biphenyl group, substituted or unsubstituted bicyclic ring, substituted or unsubstituted phenyl group and substituted or unsubstituted pyridyl.

36. A compound of claim **34**, said compound having the formula:



wherein R_p is a member selected from the group consisting of substituted or unsubstituted alkyl, substituted or unsubstituted aryl and substituted or unsubstituted heteroaryl.

37. A compound of Claim **29**, said compound having the formula (**III**):



wherein

the subscript q is an integer of from 0 to 4;

R^1 is hydrogen or a substituent having the formula $-L^1$-COOH;

X is a moiety selected from –S-, -O-, and -N(R_o)- , wherein R_o is H or lower alkyl;

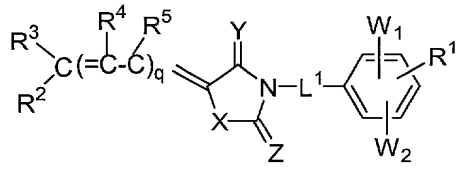
R^2 is a substituted or unsubstituted aryl(C_1-C_8)alkyl, a substituted or unsubstituted aryl(C_1-C_8)alkenyl, a substituted or unsubstituted aryl(C_1-C_8)alkynyl, a substituted or unsubstituted alicyclic group having from 5-8 carbon atoms, or a group having the formula $(R_{2a})_r$-$(L)_s$-R_{2b}-, wherein R_{2a} and R_{2b} can be the same or different and represent a substituted or unsubstituted heterocyclic group or a substituted or unsubstituted phenyl group, R_{2a} can also represent a substituted or unsubstituted polycyclic group, and L represents a divalent linking group selected from methylene, ethylene, propylene, -CH=CH-, -C≡C-, -C(O)-, -O-, -S-, -S(O)-, -S$(O)_2$-, or –N(R_{2c})-, wherein R_{2c} is selected from H or lower alkyl, and the subscripts r and s are each independently 0 or 1;

Y represents O or S; and

Z represents O, S or N(R_{2d}), wherein R_{2d} is H or lower alkyl, or R_{2d} and R^1 may be joined to form an imidazole or benzimidazole group;

with the proviso that when R^1 is hydrogen R^2 is not substituted or unsubstituted furan.

38. A compound of Claim **29**, said compound having the formula (**V**):

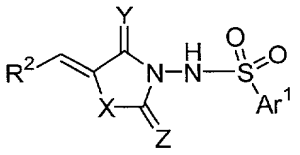


wherein

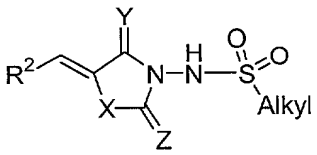
R^1 is H, -OH, -$COOR_u$, -$CONR_vR_w$, -$SO_2NR_xR_y$ wherein R_u, R_v, R_w, R_x and R_y are H or lower alkyl, or R^1 is a mono-heterocyclic group selected from furan, thiophene, pyridine, pyrimidine, pyridazine, 1,3-oxathiolane, tetrazole, oxadiazole, oxazole, triazole, imidazoline, imidazole, thiazole, thiadiazole, pyrrole, piperidine, morpholine, triazine and pyrazole; and

W_1 and W_2 are independently selected from H, (C_1-C_8)alkyl, (C_1-C_8)alkenyl, (C_1-C_8)alkynyl, halogen, nitro, hydroxy, perfluoroalkyl, difluoromethyl, (C_1-C_8)alkoxy, phenoxy, phenyl(C_1-C_8)alkoxy, (C_1-C_8)acyl, (C_1-C_8)acyloxy, cyano, carbalkoxy, thio, (C_1-C_8)alkylthio, (C_1-C_8)alkylsulfinyl, (C_1-C_8)alkylsulfonyl, amino, (C_1-C_8)alkylamino, di(C_1-C_8)alkylamino, sulfonamido, carboxamido and (C_1-C_8)alkanoylamino.

39. A compound of Claim **29**, said compound having a formula selected from the group consisting of



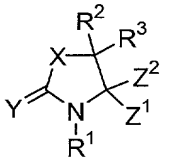
and



wherein

R^2 is a substituted or unsubstituted mono- or bi-heterocyclic group, a substituted or unsubstituted polycyclic ring, a substituted or unsubstituted alicyclic group having 5-8 carbon atoms, a substituted or unsubstituted phenyl group, a substituted or unsubstituted biphenyl group, a substituted or unsubstituted phenylether group, a substituted or unsubstituted cinnamenyl group, or a substituted or unsubstituted stilbenyl group.

40. A compound having the formula:



wherein

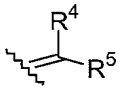
X is a member selected from the group consisting of O, S, NR^{11} and $CR^{11}R^{12}$ wherein R^{11} and R^{12} are each members independently selected from the group consisting of H, substituted or unsubstituted (C_1-C_8)alkyl, substituted or unsubstituted (C_1-C_8)alkoxy and substituted or unsubstituted (C_1-C_8)acyl;

Y is a member selected from the group consisting of O and S, or taken together with the carbon atom to which it is attached forms a methylene group;

Z^1 and Z^2 are each members independently selected from the group consisting of H and substituted or unsubstituted (C_1-C_8)alkoxy, or taken together form an oxo moiety;

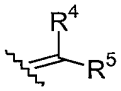
R^1 is a member selected from the group consisting of substituted or unsubstituted (C_1-C_8)alkyl, substituted or unsubstituted (C_1-C_8)alkylamino, substituted or unsubstituted di(C_1-C_8)alkylamino, substituted or unsubstituted (C_1-C_8)acylamino, amino, H, substituted or unsubstituted aryl(C_1-C_8)alkyl, substituted or unsubstituted heteroaryl(C_1-C_8)alkyl, substituted or unsubstituted heterocycloalkyl and -$NHSO_2$-Ar^1, wherein Ar^1 is selected from the group consisting of substituted or unsubstituted aryl and substituted or unsubstituted heteroaryl; and

R^2 and R^3 are each members independently selected from the group consisting of halo, substituted or unsubstituted (C_1-C_8)alkyl and substituted or unsubstituted (C_1-C_8)acyl, or taken together form a group of the formula:



wherein R^4 and R^5 are each members independently selected from the group consisting of H, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl, with the proviso that no more than one of R^4 and R^5 are H;

with the proviso that when Z^1 and Z^2 taken together form an oxo moiety and R^2 and R^3 taken together form a group of the formula:



R^1 is not substituted or unsubstituted (C_1-C_8)alkyl or H

41. A compound in accordance with claim **40**, wherein R^1 is selected from the group consisting of amino and substituted or unsubstituted -$NHSO_2$-Ar^1.

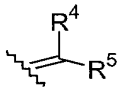
42. A compound in accordance with claim **40**, wherein Z^1 and Z^2 taken together are oxo.

43. A compound in accordance with claim **40**, wherein Y is O or S and Z^1 and Z^2 taken together are oxo.

44. A compound in accordance with claim **40**, wherein X and Y are S and Z^1 and Z^2 taken together are oxo.

45. A compound in accordance with claim **40**, wherein R^1 is selected from the group consisting of substituted or unsubstituted (C_1-C_8)alkylamino, substituted

or unsubstituted di(C_1-C_8)alkylamino, substituted or unsubstituted (C_1-C_8)acylamino, amino, and -$NHSO_2$-Ar^1, wherein Ar^1 is selected from the group consisting of substituted or unsubstituted aryl and substituted or unsubstituted heteroaryl; X and Y are each independently selected from the group consisting of O and S; Z^1 and Z^2 taken together are oxo; and R^2 and R^3 taken together are a group having the formula:



wherein R^4 and R^5 are each members independently selected from the group consisting of H, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl, with the proviso that only one of R^4 and R^5 is H.

46. A pharmaceutical composition, comprising a pharmaceutically acceptable carrier and a therapeutically or prophylactically effective amount of a compound of any one of claims **1**, **9**, **12**, **24**, **26**, **29** and **40**.

47. A method for the treatment or prevention of a viral infection, comprising

administering to a subject suffering from or at risk for said viral infection an effective amount of a compound of any one of claims **1**, **9**, **12**, **24**, **26**, **29** and **40**.

48. The method of Claim **47**, wherein said viral infection is hepatitis C virus infection.

49. The method of Claim **47**, wherein said compound is administered in combination with a therapeutically effective amount of an antiviral agent.

50. The method of Claim **49**, wherein said antiviral agent is an interferon.

51. A method for treating or preventing a viral infection, comprising

administering to a subject in need thereof a therapeutically effective amount of a compound that binds to a cysteine residue in the RNA-dependent RNA polymerase (RdRp) protein of a virus forming a covalent bond.

52. The method of Claim **51**, wherein said RdRp protein is NS5B.

53. The method of Claim **51**, wherein said viral infection is hepatitis C virus infection.

54. The method of Claim **51**, wherein said compound comprises an electrophilic group that reacts with a cysteine residue of said RdRp protein.

55. The method of Claim **54**, wherein said electrophilic group is selected from the group consisting of an activated double or triple bond, an electrophilic center, a carboxylic acid or carboxylic acid derivative, a sulfur-containing group and an activated or unactivated carbonyl group.

Patent Application Publication